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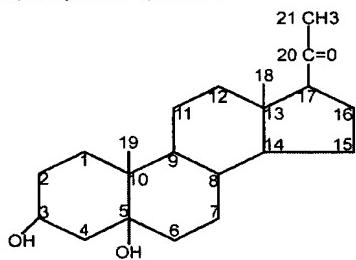
Figure 1

Cholesterol → pregnenolone →² progesterone →³ 5 β pregnane-3,20-dione
→⁴ 5 β -pregnane 3- β -ol-20-one →⁵ pregnane-3 β ,5 β -diol 20-one → hydroxylations
→ buteneolide formation → glycosylation → HIF

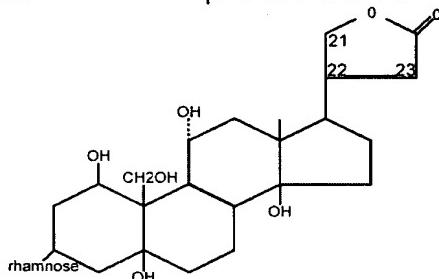
or, alternatively

Cholesterol → pregnenolone → progesterone →⁶ 5 α pregnane-3,20-dione
→⁷ 3 α -hydroxy-5 α -pregnane-20-one →⁸ 3 β hydroxy 5 α -pregnane-20-one
→ hydroxylations → buteneolide formation → glycosylation → HIF

Enzyme	OGS	Human LocusLink	Rat Orthologs on Microarray
1 Cholesterol side chain cleavage enzyme (P450, subfamily XIA)	CYP11A	1583	NM_017286
2 Δ 5-3 β -Hydroxysteroid dehydrogenase isomerase	HSD3B1 HSD3B2	3283 3284	L17138, NM_017265, NM_012584
3 5 β -Reductase	AKR1D1	6718	D17309
4 3 β -Hydroxysteroid oxidoreductase	HSD3B1 HSD3B2	3283 3284	L17138, NM_017265, NM_012584
5 5 β -Hydroxylase	unknown	NA	NA
6 5 α -Reductase	SRD5A1 SRD5A2	6715, 6716	J05035
7 3 α -Hydroxysteroid dehydrogenase/oxydoreductase	AKR1C4 AKR1C1 AKR1C2 AKR1C3	1109, 1645, 1646, 8644	L32601, D17310
8 3-Hydroxysteroid epimerase	RODH	8630	U18762, U33500, U89280

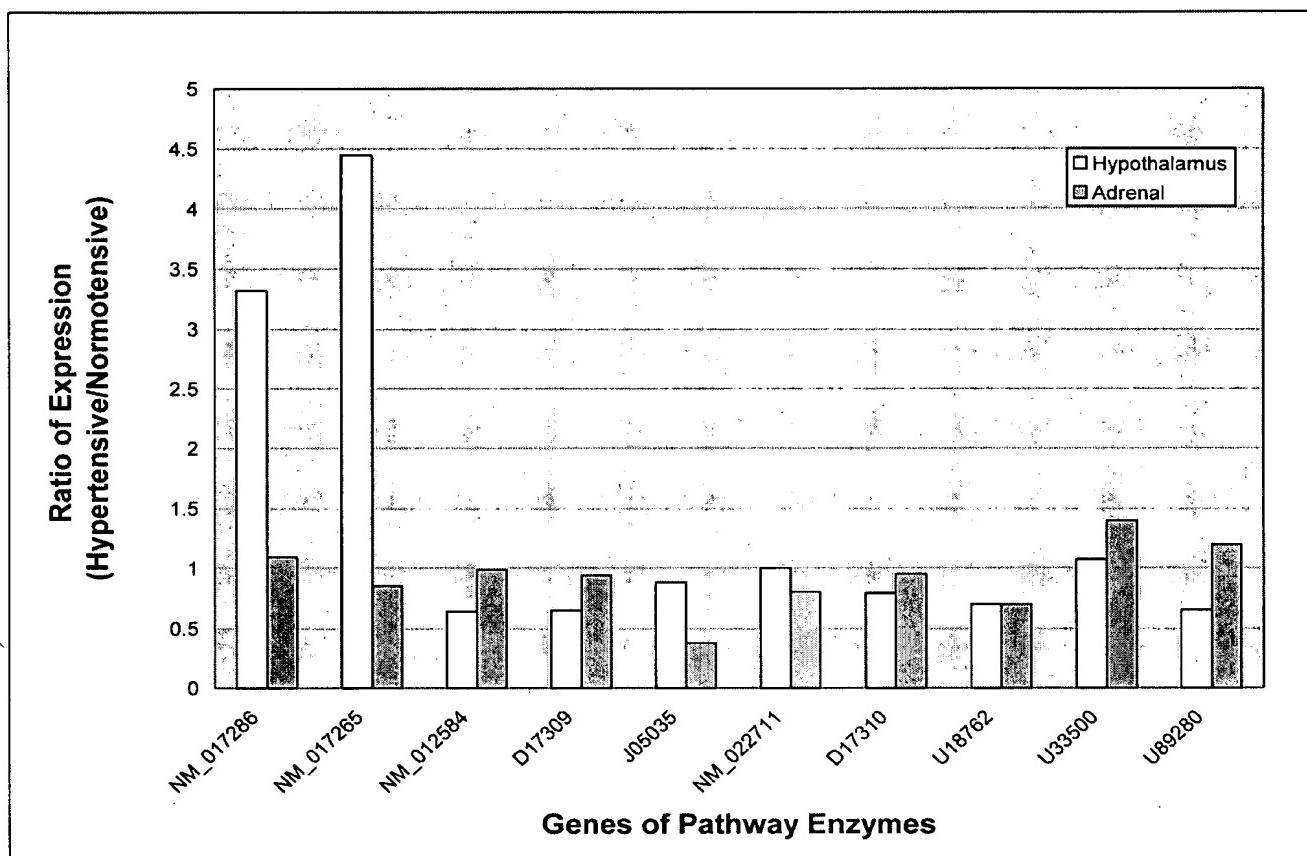


Pregnane-3 β , 5 β -diol-20one



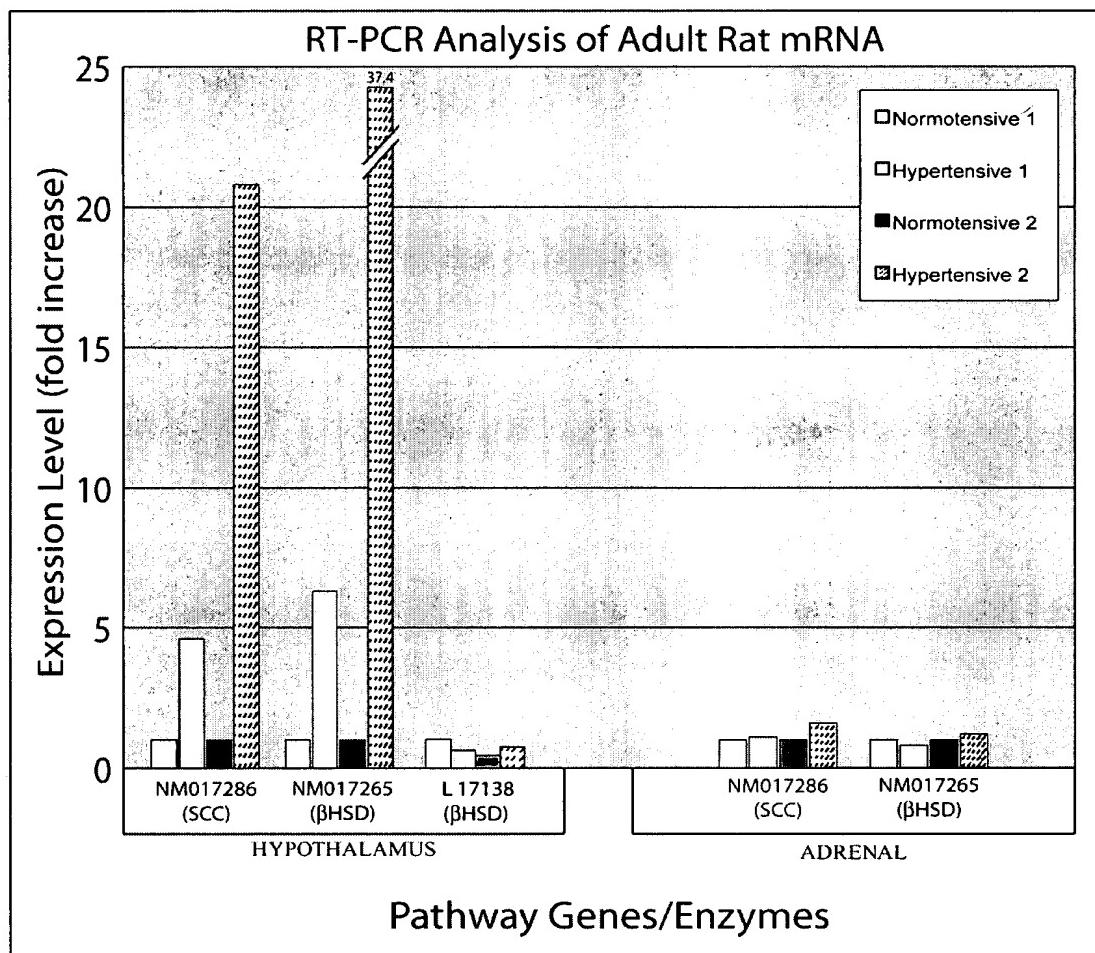
Ouabain

Figure 2



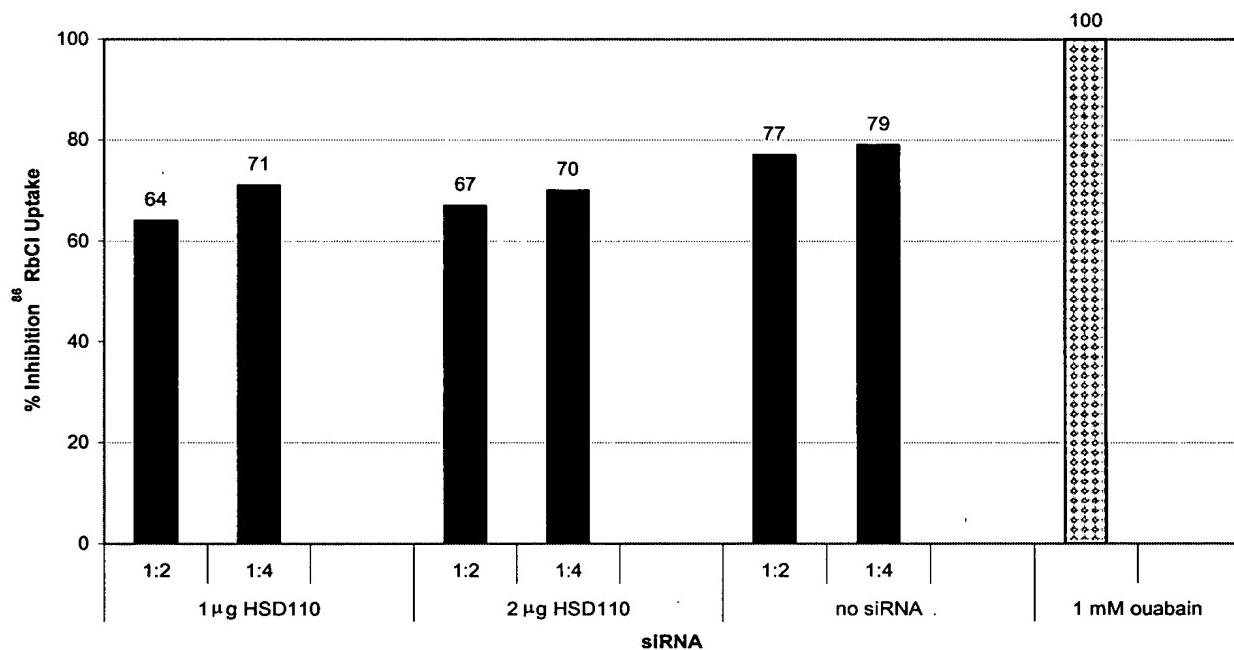
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Figure 3



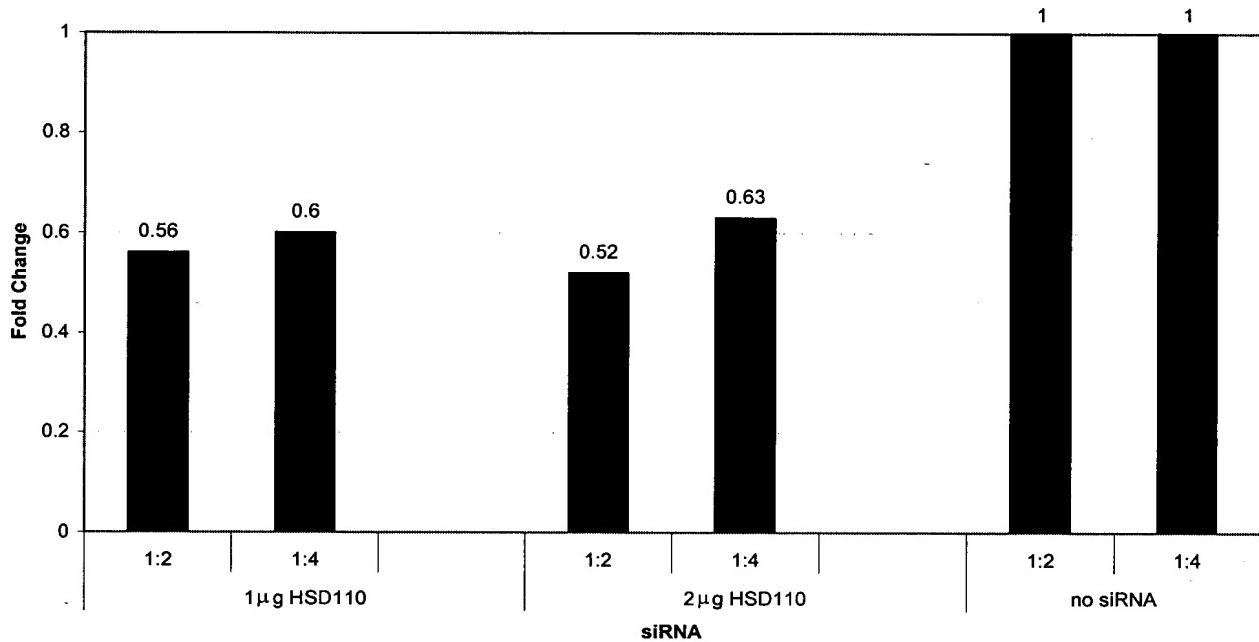
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Figure 4



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Figure 5



Docket No.: 0838.2003-001
Title: Biosynthesis of HIF
Inventors: Garner T. Haupert, Jr., *et al.*

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Figure 6

